

Amendments to the Claims:

Claim 1 (Original): A gene cassette comprising a combination of genes which, in an appropriate strain background, are able to direct the synthesis of mycaminose or angolosamine and to direct its subsequent transfer to an aglycone or pseudoaglycone.

Claim 2 (Original): A gene cassette according to claim 1, comprising a combination of genes able to direct the synthesis and transfer of mycaminose, wherein:

- a) at least one of the genes is selected from the group consisting of: *angorf14*, *tylMIII*, *tylMI*, *tylB*, *tylAI*, *tylAII*, *tylIa*, *angAI*, *angAII*, *angMIII*, *angB*, *angMI*, *eryG* and *eryK*;; and,
- b) at least one of the genes is a glycosyltransferase gene selected from the group consisting of *tylMII*, *angMII*, *desVII*, *eryCIII*, *eryBV*, *spnP*, and *midI*.

Claim 3 (Original): A gene cassette according to claim 2, wherein one of the genes within the gene cassette is *tylIa*

Claim 4 (Original): A gene cassette according to claim 2, wherein one of the genes within the gene cassette is *angorf14*

Claim 5 (Currently Amended): A gene cassette according to claim 2 ~~or 4~~, which comprises *angAI*, *angAII*, *angorf14*, *angMIII*, *angB* and *angMI*, in combination with one or more glycosyltransferase genes selected from the group consisting of *eryCIII*, *tylMII* and *angMII*.

Claim 6 (Currently Amended): A gene cassette according to claim 2 ~~or 3~~, which comprises *tylAI*, *tylAII*, *tylMIII*, *tylB*, *tylIa* and *tylMI*, in combination with one or more glycosyltransferase genes selected from the group consisting of *eryCIII*, *tylMII* and *angMII*.

Claim 7 (Original): A gene cassette according to claim 1 comprising a combination of genes able to direct the synthesis and transfer of angolosamine, wherein:

- a) at least one of the genes is selected from the group

consisting of: *angMIII*, *angMI*, *angB*, *angAI*, *angAII*, *angorf14*, *angorf4*, *tylMIII*, *tylMI*, *tylB*, *tylAI*, *tylAII*, *eryCVI*, *spnO*, *eryBVI*, and *eryK*; and,

b) at least one of the genes is a glycosyltransferase gene selected from the group consisting of *eryCIII*, *tylMII*, *angMII*, *desVII*, *eryBV*, *spnP* and *midI*.

Claim 8 (Original): A gene cassette according to claim 7, which comprises *angMIII*, *angMI*, *angB*, *angAI*, *angAII*, *angorf14* and *spnO*, in combination with one or more glycosyltransferase genes selected from the group consisting of *angMII*, *tylMII* and *eryCIII*.

Claim 9 (Original): A gene cassette according to claim 7, which comprises *angMIII*, *angMI*, *angB*, *angAI*, *angAII*, *angorf4*, and *angorf14*, in combination with one or more glycosyltransferase genes selected from the group consisting of *angMII*, *tylMII* and *eryCIII*.

Claim 10 (Currently Amended): A process for the production of erythromycins and azithromycins which contain either mycaminose or angolosamine at the C-5 position, said process comprising transforming a strain with a gene cassette ~~as described in any one of claims 1-9~~ above of claim 1 and culturing the strain under appropriate conditions for the production of said erythromycin or azithromycin.

Claim 11 (Original): The process of claim 10, wherein the strain is selected from actinomycetes, *Pseudomonas*, myxobacteria, and *E. coli*.

Claim 12 (Original): The process of claim 10, wherein the host strain is additionally transformed with the *ermE* from *S. erythraea*.

Claim 13 (Currently Amended): The process of claim 10 ~~or claim 11~~, wherein the host strain is an actinomycete.

Claim 14 (Original): The process of claim 13, wherein the host strain is selected from *S. erythraea*, *Streptomyces griseofuscus*, *Streptomyces cinnamonensis*, *Streptomyces albus*, *Streptomyces lividans*, *Streptomyces hygroscopicus* sp., *Streptomyces hygroscopicus*

var. ascomyceticus, *Streptomyces longisporoflavus*, *Saccharopolyspora spinosa*, *Streptomyces tsukubaensis*, *Streptomyces coelicolor*, *Streptomyces fradiae*, *Streptomyces rimosus*, *Streptomyces avermitilis*, *Streptomyces eurythermus*, *Streptomyces venezuelae*, and *Amycolatopsis mediterranei*.

Claim 15 (Original): The process of claim 14, wherein the host strain is *S. erythraea*.

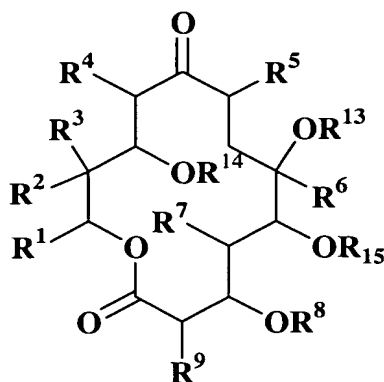
Claim 16 (Original): The process of claim 15, wherein the host strain is selected from the SGQ2, Q42/1 or 18A1 strains of *S. erythraea*.

Claim 17 (Currently Amended): The process of ~~any one of claims~~ claim 10 to 16, which further comprises feeding of an aglycone and/or a pseudoaglycone substrate to the recombinant strain.

Claim 18 (Original): The process of claim 17, wherein said aglycone and/or pseudoaglycone is selected from the group consisting of 3-O-mycarosyl erythronolide B, erythronolide B, 6-deoxy erythronolide B, 3-O-mycarosyl-6-deoxy erythronolide B, tylactone, spinosyn pseudoaglycone, 3-O-rhamnosyl erythronolide B, 3-O-rhamnosyl-6-deoxy erythronolide B, 3-O-angolosaminyl erythronolide B, 15-hydroxy-3-O-mycarosyl erythronolide B, 15-hydroxy erythronolide B, 15-hydroxy-6-deoxy erythronolide B, 15-hydroxy-3-O-mycarosyl-6-deoxy erythronolide B, 15-hydroxy-3-O-rhamnosyl erythronolide B, 15-hydroxy-3-O-rhamnosyl-6-deoxy erythronolide B, 15-hydroxy-3-O-angolosaminyl erythronolide B, 14-hydroxy-3-O-mycarosyl erythronolide B, 14-hydroxy erythronolide B, 14-hydroxy-6-deoxy erythronolide B, 14-hydroxy-3-O-mycarosyl-6-deoxy erythronolide B, 14-hydroxy-3-O-rhamnosyl erythronolide B, 14-hydroxy-3-O-rhamnosyl-6-deoxy erythronolide B, 14-hydroxy-3-O-angolosaminyl erythronolide B.

Claim 19 (Currently Amended): The process of ~~any one of claims~~ claim 10 to 18, which additionally comprises the step of isolating the compound produced.

Claim 20 (Original): A compound according to the formula I below:



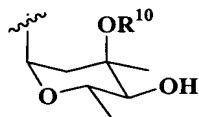
R¹ is selected from:

- H, CH₃, C₂H₅
- an alpha-branched C₃-C₈ group selected from alkyl, alkenyl, alkynyl, alkoxyalkyl and alkylthioalkyl groups any of which may be optionally substituted by one or more hydroxyl groups;
- a C₅-C₈ cycloalkylalkyl group wherein the alkyl group is an alpha-branched C₂-C₅ alkyl group
- a C₃-C₈ cycloalkyl group or C₅-C₈ cycloalkenyl group, either of which may optionally be substituted by one or more hydroxyl, or one or more C₁-C₄ alkyl groups or halo atoms
- a 3 to 6 membered oxygen or sulphur containing heterocyclic ring which may be saturated, or fully or partially unsaturated and which may optionally be substituted by one or more C₁-C₄ alkyl groups, halo atoms or hydroxyl groups
- phenyl which may be optionally substituted with at least one substituent selected from C₁-C₄ alkyl, C₁-C₄ alkoxy and C₁-C₄ alkylthio groups, halogen atoms, trifluoromethyl, and cyano or
- R¹⁷-CH₂- where R¹⁷ is H, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, alkoxyalkyl or alkylthioalkyl containing from 1 to 6 carbon atoms in each alkyl or alkoxy group wherein any of said alkyl, alkoxy, alkenyl or alkynyl groups may be substituted by one or more hydroxyl groups or by one or more halo atoms; or a C₃-C₈ cycloalkyl or C₅-C₈ cycloalkenyl either of which may be optionally

substituted by one or more C₁-C₄ alkyl groups or halo atoms; or a 3 to 6 membered oxygen or sulphur containing heterocyclic ring which may be saturated or fully or partially unsaturated and which may optionally be substituted by one or more C₁-C₄ alkyl groups or halo atoms; or a group of the formula SA₁₆ wherein A₁₆ is C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, phenyl or substituted phenyl wherein the substituent is C₁-C₄ alkyl, C₁-C₄ alkoxy or halo, or a 3 to 6 membered oxygen or sulphur-containing heterocyclic ring which may be saturated, or fully or partially unsaturated and which may optionally be substituted by one or more C₁-C₄ alkyl groups or halo atoms

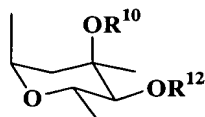
R², R⁴, R⁵, R⁶, R⁷ and R⁹ are each independently H, OH, CH₃, C₂H₅ or OCH₃

R³ = H or OH



R⁸ = H, , rhamnose, 2'-O-methyl rhamnose, 2',3'-bis-O-methyl rhamnose, 2',3',4'-tri-O-methyl rhamnose, oleandrose, olioside, digitoxose, olivose or angolosamine;

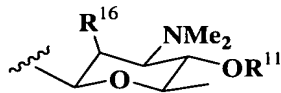
R¹⁰ = H or CH₃ or C(=O)R_A, where R_A = C₁-C₆ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl



R¹¹ = H, , mycarose, C4-O-acyl-mycarose or glucose

R¹² = H or C(=O)R_A, where R_A = C₁-C₆ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl

R¹³ = H or CH₃



R¹⁵ = H or

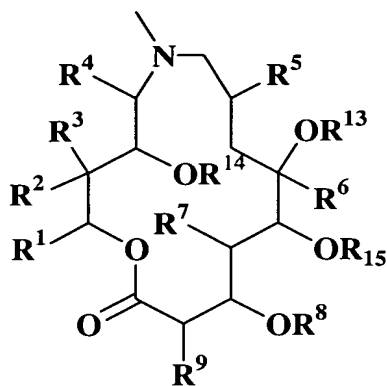
R¹⁶ = H or OH

R¹⁴ = H or -C(O)NR^cR^d wherein each of R^c and R^d is independently H, C₁-C₁₀ alkyl, C₂-C₂₀ alkenyl, C₂-C₁₀ alkynyl, -(CH₂)_m(C₆-C₁₀ aryl), or -(CH₂)_m(5-10 membered heteroaryl), wherein m is an integer ranging from 0 to 4, and wherein each of the foregoing R^c and R^d groups, except H, may be substituted by 1 to 3 Q groups; or wherein R^c and R^d

may be taken together to form a 4-7 membered saturated ring or a 5-10 membered heteroaryl ring, wherein said saturated and heteroaryl rings may include 1 or 2 heteroatoms selected from O, S and N, in addition to the nitrogen to which R^c and R^d are attached, and said saturated ring may include 1 or 2 carbon-carbon double or triple bonds, and said saturated and heteroaryl rings may be substituted by 1 to 3 Q groups; or R² and R¹⁷ taken together form a carbonate ring; each Q is independently selected from halo, cyano, nitro, trifluoromethyl, azido, -C(O)Q¹, -OC(O)Q¹, -C(O)OQ¹, -OC(O)OQ¹, -NQ²C(O)Q³, -C(O)NQ²Q³, -NQ²Q³, hydroxy, C₁-C₆ alkyl, C₁-C₆ alkoxy, -(CH₂)_m(C₆-C₁₀ aryl), and -(CH₂)_m(5-10 membered heteroaryl), wherein m is an integer ranging from 0 to 4, and wherein said aryl and heteroaryl substituents may be substituted by 1 or 2 substituents independently selected from halo, cyano, nitro, trifluoromethyl, azido, -C(O)Q¹, -C(O)OQ¹, -OC(O)OQ¹, -NQ²C(O)Q³, -C(O)NQ²Q³, -NQ²Q³, hydroxy, C₁-C₆ alkyl, and C₁-C₆ alkoxy;

each Q¹, Q² and Q³ is independently selected from H, OH, C₁-C₁₀ alkyl, C₁-C₆ alkoxy, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, -(CH₂)_m(C₆-C₁₀ aryl), and -(CH₂)_m(5-10 membered heteroaryl), wherein m is an integer ranging from 0 to 4; with the proviso that the compound is not 5-O-dedesosaminy-5-O-mycaminosyl erythromycin A or D or said compound is a variant of any of the above in which the -CHOR¹⁴- at C11 is replaced by a methylene group (-CH₂-), a keto group (C=O), or by a 10,11-olefinic bond; or said compound is a variant of any of the above which differs in the oxidation state of one or more of the ketide units (i.e. selection of alternatives from the group: -CO-, -CH(OH)-, alkene -CH-, and CH₂); with the proviso that the compounds are not selected from the group consisting of 5-O-dedesosaminy-5-O-mycaminosyl erythromycin A and 5-O-dedesosaminy-5-O-mycaminosyl erythromycin D.

Claim 21 (Original): A compound according to the formula II below:



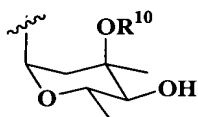
R¹ is selected from:

- H, CH₃, C₂H₅
- an alpha-branched C₃-C₈ group selected from alkyl, alkenyl, alkynyl, alkoxyalkyl and alkylthioalkyl groups any of which may be optionally substituted by one or more hydroxyl groups;
- a C₅-C₈ cycloalkylalkyl group wherein the alkyl group is an alpha-branched C₂-C₅ alkyl group
- a C₃-C₈ cycloalkyl group or C₅-C₈ cycloalkenyl group, either of which may optionally be substituted by one or more hydroxyl, or one or more C₁-C₄ alkyl groups or halo atoms
- a 3 to 6 membered oxygen or sulphur containing heterocyclic ring which may be saturated, or fully or partially unsaturated and which may optionally be substituted by one or more C₁-C₄ alkyl groups, halo atoms or hydroxyl groups
- phenyl which may be optionally substituted with at least one substituent selected from C₁-C₄ alkyl, C₁-C₄ alkoxy and C₁-C₄ alkylthio groups, halogen atoms, trifluoromethyl, and cyano or
- R¹⁷-CH₂- where R¹⁷ is H, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, alkoxyalkyl or alkylthioalkyl containing from 1 to 6 carbon atoms in each alkyl or alkoxy group wherein any of said alkyl, alkoxy, alkenyl or alkynyl groups may be substituted by one or more hydroxyl groups or by one or more halo atoms; or a C₃-C₈ cycloalkyl or C₅-C₈

cycloalkenyl either of which may be optionally substituted by one or more C₁-C₄ alkyl groups or halo atoms; or a 3 to 6 membered oxygen or sulphur containing heterocyclic ring which may be saturated or fully or partially unsaturated and which may optionally be substituted by one or more C₁-C₄ alkyl groups or halo atoms; or a group of the formula SA₁₆ wherein A₁₆ is C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, phenyl or substituted phenyl wherein the substituent is C₁-C₄ alkyl, C₁-C₄ alkoxy or halo, or a 3 to 6 membered oxygen or sulphur-containing heterocyclic ring which may be saturated, or fully or partially unsaturated and which may optionally be substituted by one or more C₁-C₄ alkyl groups or halo atoms

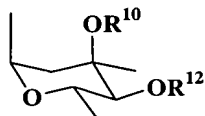
R², R⁴, R⁵, R⁶, R⁷ and R⁹ are each independently H, OH, CH₃, C₂H₅ or OCH₃

R³ = H or OH



R⁸ = H, , rhamnose, 2'-O-methyl rhamnose, 2',3'-bis-O-methyl rhamnose, 2',3',4'-tri-O-methyl rhamnose, oleandrose, oliose, digitoxose, olivose or angolosamine;

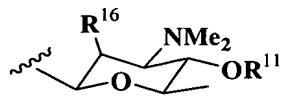
R¹⁰ = H or CH₃ or C(=O)R_A, where R_A = C₁-C₆ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl



R¹¹ = H, , mycarose, C4-O-acyl-mycarose or glucose

R¹² = H or C(=O)R_A, where R_A = C₁-C₆ alkyl, C₂-C₆ alkenyl or C₂-C₆ alkynyl

R¹³ = H or CH₃



R¹⁵ = H or

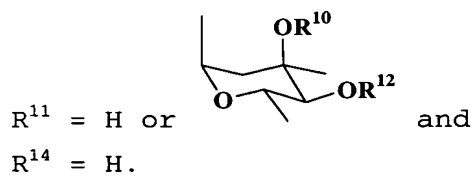
R¹⁶ = H or OH

R¹⁴ = H or -C(O)NR^cR^d wherein each of R^c and R^d is independently H, C₁-C₁₀ alkyl, C₂-C₂₀ alkenyl, C₂-C₁₀ alkynyl, -(CH₂)_m(C₆-C₁₀ aryl), or -(CH₂)_m(5-10 membered heteroaryl), wherein m is an integer ranging from 0 to 4, and wherein each of the foregoing R^c and R^d groups,

except H, may be substituted by 1 to 3 Q groups; or wherein R^c and R^d may be taken together to form a 4-7 membered saturated ring or a 5-10 membered heteroaryl ring, wherein said saturated and heteroaryl rings may include 1 or 2 heteroatoms selected from O, S and N, in addition to the nitrogen to which R^c and R^d are attached, and said saturated ring may include 1 or 2 carbon-carbon double or triple bonds, and said saturated and heteroaryl rings may be substituted by 1 to 3 Q groups; or R² and R¹⁷ taken together form a carbonate ring; each Q is independently selected from halo, cyano, nitro, trifluoromethyl, azido, -C(O)Q¹, -OC(O)Q¹, -C(O)OQ¹, -OC(O)OQ¹, -NQ²C(O)Q³, -C(O)NQ²Q³, -NQ²Q³, hydroxy, C₁-C₆ alkyl, C₁-C₆ alkoxy, -(CH₂)_m(C₆-C₁₀ aryl), and -(CH₂)_m(5-10 membered heteroaryl), wherein m is an integer ranging from 0 to 4, and wherein said aryl and heteroaryl substituents may be substituted by 1 or 2 substituents independently selected from halo, cyano, nitro, trifluoromethyl, azido, -C(O)Q¹, -C(O)OQ¹, -OC(O)OQ¹, -NQ²C(O)Q³, -C(O)NQ²Q³, -NQ²Q³, hydroxy, C₁-C₆ alkyl, and C₁-C₆ alkoxy; each Q¹, Q² and Q³ is independently selected from H, OH, C₁-C₁₀ alkyl, C₁-C₆ alkoxy, C₂-C₁₀ alkenyl, C₂-C₁₀ alkynyl, -(CH₂)_m(C₆-C₁₀ aryl), and -(CH₂)_m(5-10 membered heteroaryl), wherein m is an integer ranging from 0 to 4; or said compound is a variant of any of the above in which the -CHOR¹⁴- at C12 is replaced by a methylene group (-CH₂-), a keto group (C=O), or by a 11,12-olefinic bond; or said compound is a variant of any of the above which differs in the oxidation state of one or more of the ketide units (i.e. selection of alternatives from the group: -CO-, -CH(OH)-, alkene -CH-, and CH₂).

Claim 22 (Currently Amended): A compound according to claim 20 or 21, wherein: R², R⁴, R⁵, R⁶, R⁷ and R⁹ are all CH₃.

Claim 23 (Currently Amended): A compound according to claim 22, wherein



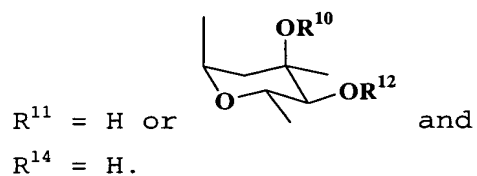
Claim 24 (Currently Amended): A compound according to claim 23, wherein $R^1 = C_2H_5$ optionally substituted with a hydroxyl group.

Claim 25 (Currently Amended): A compound according to claim 24, wherein $R^{12} = H$.

Claim 26 (Currently Amended): A compound according to claim 25, wherein $R^1 = C_2H_5$.

Claim 27 (New): A compound according to claim 21, wherein: R^2 , R^4 , R^5 , R^6 , R^7 and R^9 are all CH_3 .

Claim 28 (New): A compound according to claim 27, wherein



Claim 29 (New): A compound according to claim 28, wherein $R^1 = C_2H_5$ optionally substituted with a hydroxyl group.

Claim 30 (New): A compound according to claim 29, wherein $R^{12} = H$.

Claim 31 (New): A compound according to claim 25, wherein $R^1 = C_2H_5$.